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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/782,040	02/19/2004	Tsugumori Notomi	201487/1024 (E2-001PCT-US)	5624
7590	09/19/2007		EXAMINER	
Edwin V. Merkel Nixon Peabody LLP Clinton Square P.O. Box 31051 Rochester, NY 14603-1051			BABIC, CHRISTOPHER M	
			ART UNIT	PAPER NUMBER
			1637	
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			09/19/2007	PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/782,040	<b>Applicant(s)</b> NOTOMI ET AL.	
	<b>Examiner</b> Christopher M. Babic	<b>Art Unit</b> 1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) ☒ Responsive to communication(s) filed on 02 July 2007.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) ☒ Claim(s) 54-59 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 54-59 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)                                | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                       | 5) <input type="checkbox"/> Notice of Informal Patent Application                       |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

## **DETAILED ACTION**

### ***Status of the Claims***

Claim(s) 20, 22, and 54-59 are pending. The following Office Action is in response to Applicant's response dated July 2, 2007.

### ***Election/Restrictions***

Applicant has requested the withdrawal of the restriction requirement issued April 16, 2006. Applicant is reminded that because Applicant did not **distinctly and specifically** point out the supposed errors in the restriction requirement in the election response filed November 8, 2006, the has been treated as an election filed on **without traverse** (MPEP § 818.03(a)). The restriction requirement was therefore considered FINAL and claim(s) 20 and 22 were withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention.

### ***Claim Interpretation***

Applicant's arguments with regard to the interpretation of the term --3' terminal sequence-- and --5' terminal sequence-- have been fully considered and are persuasive. Therefore, the rejections based in part on the interpretation have been withdrawn. However, as pointed out by Applicant, the above terms will be considered to require, at the least, **two nucleotides**. Applicant is further reminded that the claimed invention **does not require** a 5- terminal nucleotide sequence that contributes to loop formation

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at the 3' end of an extension product. This particular interpretation has certain implications with regard to the prior art applied below (see sections 35 USC 102 and 103 below).

***New Grounds of Claim Rejections - 35 USC § 112 - Indefiniteness***

The following new ground(s) of rejection is made in view of a newly discovered indefiniteness within the claimed invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

**Claim(s) 54-59 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.**

The above claims are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: an active step of synthesizing a nucleic acid molecule. The claim requires a mixing step as well as an incubation step that only requires stable base pairing. The lack an active step of synthesizing amounts to a lack of a nexus between the claimed active steps of the method and the intended goal of the preamble.

***New Grounds of Claim Rejections - 35 USC § 102***

The following new grounds of rejections are made in view of previously considered prior art.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

**Claim(s) 54, 58, and 59 are rejected under 35 U.S.C. 102(b) as being anticipated by Cleuziat et al. (WO 95/03426 A2; 2 February 1995; 02.02.95) as evidenced by the English translation provided in Cleuziat et al. (U.S. 5,849,547).**

With regard to claim(s) 54, Cleuziat teaches a method (*fig. 15; example 5, col. 33-35; col. 33, lines 35-45, col. 34, lines 60-col. 35, Cleuziat teaches an amplification reaction containing two inner primers, SEQ ID NO: 12,13, and two outer displacement primers, SEQ ID NO: 10,16, for example*) comprising: A) mixing the following components 1) to 3) with sample nucleic acid as a template (*col. 33-35, SEQ ID NO: 1, for example*) 1) a primer set consisting of four distinct oligonucleotide primers, wherein: the first oligonucleotide primer comprises (i) a 3' terminal nucleotide sequence that anneals to a sample single-stranded nucleic acid molecule and serves as the origin of

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synthesis for synthesizing a first single-stranded nucleic acid molecule complementary at least in part to the sample single-stranded nucleic acid molecule and (ii) a 5' terminal nucleotide sequence that is complementary to an arbitrary region of the first single-stranded nucleic acid molecule (*col. 33-35, SEQ ID NO: 12, 5' terminal nucleotides 1-3 TCT, complementary to nucleotides 48-50 AGA, for example*); the second oligonucleotide primer comprises (i) a 3' terminal nucleotide sequence that anneals to the first single-stranded nucleic acid molecule prepared using the first oligonucleotide primer and serves as the origin of synthesis for synthesizing a second single-stranded nucleic acid molecule complementary at least in part to the first single-stranded nucleic acid molecule, and (ii) a 5' terminal nucleotide sequence that is complementary to an arbitrary region of the second single-stranded nucleic acid molecule (*col. 33-35, SEQ ID NO: 13, 5' terminal nucleotides 1-3 TCT, complementary to nucleotides 48-50 AGA, for example*); the third oligonucleotide primer comprises a nucleotide sequence which anneals to a region of the sample single-stranded nucleic acid molecule, wherein said region is located 3' to a region where the first oligonucleotide primer anneals and outside of a region defined by the outer nucleotides of the first oligonucleotide primer (*col. 33-35, SEQ ID NO: 10, for example*); and the fourth oligonucleotide primer comprises a nucleotide sequence which anneals to a region of the first single-stranded nucleic acid molecule, wherein said region is located 3' to a region where the second oligonucleotide primer anneal and outside of a region defined by the outer nucleotides of the first oligonucleotide primer (*col. 33-35, SEQ ID NO: 16, for example*); 2) a DNA polymerase having strand displacement activity (defined by the outer nucleotides of the

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first oligonucleotide primer (*col. 33-35, MMLV reverse transcriptase, for example*)); and 3) one or more nucleotides which are used by the DNA polymerase to extend the primers (defined by the outer nucleotides of the first oligonucleotide primer (*col. 33-35, ATP, etc., for example*)); and B) incubating the mixture at such a temperature that the nucleotide sequence constituting the first and third oligonucleotide primers can form stable base with the template (defined by the outer nucleotides of the first oligonucleotide primer (*col. 33-35, incubation, for example*)).

With regard to claim(s) 58, Cleuziat teaches a detector for detection of products (*col. 27, lines 35-55, UV detection, for example*).

With regard to claim(s) 59, Cleuziat teaches reverse transcription of RNA (*col. 20, lines 45-65, for example*).

### ***New Grounds of Claim Rejections - 35 USC § 103***

The following new grounds of rejections are made in view of previously considered prior art.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of

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the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

**Claim(s) 55-57 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cleuziat et al. (WO 95/03426 A2; 2 February 1995; 02.02.95) as evidenced by the English translation provided in Cleuziat et al. (U.S. 5,849,547) as applied to claim(s) 54, 58, and 59 above, and further in view of Bloch (U.S. 5,972,618).**

With regard to claim(s) 55-57, the methods of the previously applied reference(s) have been outlined in the above rejections. The previously applied reference(s) do not expressly teach the use of melting temperature regulators.

It is submitted that melting temperature regulators, i.e. Betaine, were well known in the art at the time the claimed invention was made as taught by Bloch. Bloch teaches high concentrations of Betaine (col. 12, lines 40-63, 2-3M, for example) are preferred PCR sensitivity enhancers because it improves polymerase-template interaction without enzyme inhibition (col. 4, lines 49-60, for example).

Thus, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to add Betaine to the polymerase reactions of



Cleuziat for the expected benefit of improved polymerase-template interaction without enzyme inhibition as taught by Bloch.

***Claim Rejections - Double Patenting***

The rejections of claim(s) 54 over U.S. 6,410,278 and U.S. 6,974,670 have been withdrawn in view of the timely filed terminal disclaimers.

***Conclusion***

**Claim(s) 54-59 are rejected. No claims are allowed.**

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christopher M. Babic whose telephone number is 571-272-8507. The examiner can normally be reached on Monday-Friday 7:00AM to 4:00PM.

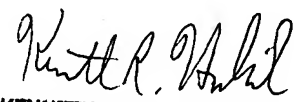
If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571-272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

 9/17/07

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